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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,802	12/26/2001	Marc Zabeau	29314/34158A	2002

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	11

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,802	ZABEAU ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *24-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (Claims 1-23) in Paper No. 10, filed on July 14, 2003 is acknowledged. Claims 1-36 are pending; claims 24-36 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821; and claims 1-23 have been examined herein and are rejected.

Sequence Notes

2. The Sequence Listing filed in this application complies with the requirements of 37 CFR 1.821-1.825 and has been entered.

Information Disclosure Statement

3. The information disclosure statement of Paper No. 5 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

Claim Objections

4. Claim 2 is objected to because the claim recites, "The method of claim 1 the concomitantly", which should be amended to recite, "The method of claim 1 **wherein** the concomitantly".

5. Claims 7 and 15 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Claims 7 and 15 have been examined to the extent that they are limited to methods depending from Claim 1. In the response to this action, the claims should be amended to depend from only one claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-10 and 12-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Zabeau et al. (EP 534858 A1, cited in the IDS).

With respect to Claims 1 and 12, Zabeau teaches a method for detecting an endonuclease site polymorphism in DNA comprising:

a) isolating sample DNA;

b) deriving a set of concomitantly amplifiable target DNA fragments from the sample DNA;

c) treating the target DNA fragments obtained in step (b) with a probe restriction endonuclease reagent;

d) amplifying the probe restriction endonuclease reagent treated target DNA fragments of step c);

e) analyzing the DNA of step d) to determine which target fragments are amplified and/or which target fragments are not amplified; and wherein target DNA fragments which are amplified lack a recognition sire for the probe restriction endonuclease reagent and target fragments having a recognition site for the probe restriction endonuclease reagent are not amplified.

(see abstract, pg. 3, lines 20-46 and pgs. 6-11, for example)

With respect to Claims 2-5, Zabeau teaches the concomitantly amplifiable target DNA fragments of step b) are "derived" by treatment of four and six base cutting endonucleases (see Examples 2-6, for example).

With respect to Claims 2-5, it is noted that step c)'s "treating" step can be interpreted as either adding an additional endonuclease or the treatment of the target DNA fragments with endonucleases already present in the assay. For example, Zabeau teaches that following the derivation of the concomitantly amplifiable target DNAs using a first and a second restriction endonuclease and the ligation of adaptors, the restriction endonucleases are still active and thus the target DNAs are still being "treated" with the endonucleases (see pg. 14, ln. 35-37) (see also pg. 18, lines 1-3 and pgs. 21, lines 53 to pg. 22, teaching two distinct treatment steps).

With respect to Claim 6, Zabeau teaches preparing primers, which flank the endonuclease site polymorphism (ESP) for use in amplifying, said concomitantly amplifiable target DNA fragments (pgs. 6-9, for example).

With respect to Claims 7 and 15-16, Zabeau teaches the concomitantly amplifiable DNA fragments are modified by the ligation of adapters to both termini of said fragments and then amplified by PCR (see pg.6 and Examples 2-6, for example).

With respect to Claim 8, Zabeau teaches the ligation of adaptors (pg. 6, for example).

With respect to Claims 9-10, Zabeau teaches the probe restriction endonuclease has a recognition sequence of four or six nucleotides (see Examples 2-6).

With respect to Claims 13-14, it is an inherent property that that the site polymorphism will is an alteration which is either recognized and cut by the probe restriction endonuclease reagent or eliminates a recognition sequence for said probe restriction endonuclease reagent.

With respect to Claim 17, Zabeau teaches that the amplified products are hybridized to probes (pg. 11, for example).

With respect to Claims 18-23, the broadest reasonable interpretation is that the claims are drawn to any probe DNA fragment having an ESP, which comprises any fragment susceptible to endonuclease digestion.

Specifically, with respect to Claims 18-19, Zabeau teaches the probe DNA fragments are derived by digestion of sample DNA with one or more sampling restriction endonuclease reagents (see Examples 2-6).

With respect to Claims 20-23, the DNA fragments are derived by digestion of a pool of sample DNAs obtained from a plurality of individuals (see abstract, Examples 5-6 and pg. 8, for example).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zabeau et al. (EP 534858 A1, cited in the IDS), as applied to claims 1-10 and 12-23 above, and further in view of Wang et al. (Science (1998) 280: 1077-1081, cited in the IDS), and further in view of Mead et al. (WO 94/21663, cited in the IDS).

The teachings of Zabeau are presented above. Specifically, Zabeau teaches a method for detecting an endonuclease site polymorphism in DNA comprising using probe restriction endonucleases having recognition sequences of short nucleotide sequences, but Zabeau does not teach restriction endonucleases having recognition sequences of 2 nucleotides.

Wang teaches a high percentage of single nucleotide polymorphisms occur within CpG dinucleotides, and thus the analysis of CpG dinucleotides are advantageous in detecting polymorphisms (see pg. 1078).

Mead teaches digesting DNA with a probe restriction endonuclease reagent, CGase I, which cleaves DNA at the dinucleotide CpG (see pgs. 1 and 77, for example).

Accordingly, in view of the teachings of Wang and Mead, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Zabeau so as to have treated a target DNA fragment with a probe restriction endonuclease reagent having a recognition sequence of two nucleotides, such as CGase I, in order to have achieved the benefit of providing a more effective means of detecting single nucleotide polymorphisms due to the high level of polymorphisms located within CpG dinucleotides.

Conclusion

12. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (703) 308-2199. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
October 28, 2003

CARLA J. MYERS
PRIMARY EXAMINER